Finding common ground

Identification of successful treatments for autoimmune diseases such as psoriasis and multiple sclerosis (MS) has proved challenging, despite the fact that both are associated with pathogenic T helper type 1 (Th1) and Th17 cells. Dimethylfumarate (DMF) is a unique small molecule that improves both psoriasis and MS. To explore the underlying mechanism of the therapeutic effect of DMF, Ghoreschi and colleagues examined human and mouse immune responses *in vitro* and *in vivo*. DMF depleted cellular glutathione and induced the generation of type II dendritic cells (DCs), which produced IL-10 as opposed to IL-12 or IL-23. These effects were mediated via interference with both the hemoxygenase-1 and the STAT1 signaling pathways. Type II DCs ultimately inhibited development of Th1/Th17 cells and induced the development of Th2 cells. Interestingly, these immunologic effects protected DMF-treated mice from developing experimental autoimmune encephalomyelitis. Thus, therapy with this small molecule improves these autoimmune diseases via interference with IL-12 and IL-23 production. (*J Exp Med* 208:2291–303, 2011) *Selected by T. Schwarz*

From adult to neonate

Typically, hair follicle morphogenesis occurs during late embryonic and early neonatal development. Although adult skin does not usually give rise to new follicles, epidermal activation of Wnt/β-catenin induces hair follicle neogenesis in adult mouse skin. The involvement of Wnt/β-catenin in this process is of interest because this factor has been implicated in epithelial cancers. Using PdgfraEGFP reporter mice, Collins and colleagues isolated pure populations of dermal fibroblasts and performed gene expression profiling studies with them. These studies revealed that neonatal dermal fibroblasts have a distinct gene expression profile. In addition, adult dermal fibroblasts could actually be reprogrammed to a neonatal state by activating β-catenin in the epidermis. This reprogramming resulted in fibroblast proliferation and extracellular matrix remodeling. Spatially, these changes were associated with fibroblasts at the hair follicle junctional zone. Taken together, these results indicate that the dermal niche, which is involved in epidermal differentiation, is a dynamic entity that responds to external cues with substantial remodeling. (*Development* 138:5189–99, 2011) *Selected by G. Cotsarelis*

Chew the fat

Although studies have examined the stem cells as well as the extrinsic signals that function in the hair follicle, the cells that establish the skin stem cell niche are not known. Festa and colleagues identified adipose precursor cells within the skin and discovered a dynamic adipogenesis process that parallels hair follicle stem cell activation. In studies of adipocyte lineage cells in mice with defects in adipogenesis, these researchers found that immature adipocytes are both necessary and sufficient to induce follicular stem cell activation and to initiate hair growth. Furthermore, defective platelet-derived growth factor (PDGF) signaling was observed in follicles without adipocyte regeneration, indicating that intradermal adipocyte precursor cells activate PDGF signaling in the dermal papillae. These results show that adipocyte lineage cells form a niche in the skin to regulate epithelial stem cell activity. (*Cell* 146:761–71, 2011) *Selected by M. Amagai*

Take the good and the bad

Cross-talk between the immune system and tissue epithelia regulates defense mechanisms in response to pathogens. In a recent study by Ramirez-Carrozzi and colleagues, IL-17C, an IL-17 family member, was found to be induced rapidly in epithelial cells in response to stimulation with bacteria or with the proinflammatory factors IL-1β and tumor necrosis factor. IL-17C required binding to IL-17RA and IL-17RE to function. Interestingly, IL-17C exhibited both protective and pathogenic functions *in vivo*. This cytokine controlled homeostasis in the gut mucosa and therefore protected against dextran sulfate sodium–induced colitis in mice. In contrast, IL-17C promoted an inflammatory pathogenic skin phenotype. Overall, these studies demonstrate that IL-17C, which is similar but not redundant to the well-studied family member IL-17A, functions in an autocrine manner to initiate an important innate immune response in the epithelium upon bacterial stimulation. Furthermore, the IL-17C pathway highlights a previously unknown mechanism for epithelium participation in host defense. (*Nat Immunol* 12:1159–66, 2011) *Selected by L. Beck*

Professional IL-17-producing cells

Accumulating evidence suggests that the IL-23/Th17 cell axis and associated cytokines are primary players in the pathogenesis of psoriasis; however, the IL-17-producing cells responsive to IL-23 stimulation in the skin are not known. Cai and colleagues found that dermal γδ T cells in the skin of mice are the major source of IL-17 following IL-23 stimulation. These cells were required for IL-23- and imiquimod-induced skin inflammation and acanthosis because mice lacking either the T cell receptor δ or the IL-17 receptor exhibited decreased hyperplasia and inflammation. In addition, IL-17-secreting γδ T cells were present in high numbers in psoriatic skin lesions in humans. Thus, in both mice and humans, dermal γδ T cells are the essential IL-17-producing cells that promote the development and progression of skin inflammation and consequently underlie psoriasis pathogenesis. (*Immunity* 35:596–610, 2011) *Selected by L. Beck*

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